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Field of the Invention

At page 1, before the second full paragraph, which begins "Cell growth is regulated by ...", please insert the following heading:

Q³

Background of the Invention

At page 4, before the first full paragraph, which begins "The following drawings are...", please insert the following heading:

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Brief Description of the Drawings

At page 4, please delete the second full paragraph, which begins "Figures 1 depicts the...", and replace therewith the following paragraph:

Figures 1A-B depict the cDNA sequence (SEQ ID NO:1) and corresponding deduced amino acid sequence (SEQ ID NO:2) of HDGF-2. The standard one letter abbreviation for amino acids is used. Sequencing was performed using a 373 Automated DNA sequencer (Applied Biosystems, Inc.).

At page 4, please delete the fourth full paragraph, which begins "In accordance with an aspect...", and replace therewith the following paragraph:

In accordance with an aspect of the present invention, there is provided an isolated nucleic acid (polynucleotide) which encodes for the mature polypeptide having the deduced amino acid sequence of Figures 1A-B (SEQ ID NO:2) or for the mature polypeptide encoded by the cDNA of the clone deposited with the American Type Culture Collection (ATCC, located at 10801 University Boulevard, Manassas, Virginia 20110-2209) as ATCC Deposit No. 97163 on May 24, 1995.

At page 4, please delete the sixth paragraph, extending onto page 5, which begins "The polynucleotide of the present...", and replace therewith the following paragraph:

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The polynucleotide of the present invention may be in the form of RNA or in the form of DNA, which DNA includes cDNA, genomic DNA, and synthetic DNA. The DNA may be double-stranded or single-stranded, and if single stranded may be the coding strand or non-coding (anti-sense) strand. The coding sequence which encodes the mature polypeptide may be identical to the coding sequence shown in Figures 1A-B (SEQ ID NO:1) or that of the deposited clone or may be a different coding sequence which coding sequence, as a result of the redundancy or degeneracy of the genetic code, encodes the same mature polypeptide as the DNA of Figures 1A-B (SEQ ID NO:1) or the deposited cDNA.

At page 5, please delete the first full paragraph, which begins "The polynucleotide which encodes...", and replace therewith the following paragraph:

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The polynucleotide which encodes for the mature polypeptide of Figures 1A-B (SEQ ID NO:2) or for the mature polypeptide encoded by the deposited cDNA may include, but is not limited to: only the coding sequence for the mature polypeptide; the coding sequence for the mature polypeptide and additional coding sequence; the coding sequence for the mature polypeptide (and optionally additional coding sequence) and non-coding sequence, such as introns or non-coding sequence 5' and/or 3' of the coding sequence for the mature polypeptide.

At page 5, please delete the third full paragraph, which begins "The present invention further relates...", and replace therewith the following paragraph:

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The present invention further relates to variants of the hereinabove described polynucleotides which encode for fragments, analogs and derivatives of the polypeptide having the deduced amino acid sequence of Figures 1A-B (SEQ ID NO:2) or the polypeptide encoded by the cDNA of the deposited clone. The variant of the polynucleotide may be a naturally occurring allelic variant of the polynucleotide or a non-naturally occurring variant of the polynucleotide.

At page 5, please delete the fourth full paragraph, which begins "Thus, the present invention includes ...", and replace therewith the following paragraph:

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Thus, the present invention includes polynucleotides encoding the same mature polypeptide as shown in Figures 1A-B (SEQ ID NO:2) or the same mature polypeptide

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encoded by the cDNA of the deposited clone as well as variants of such polynucleotides which variants encode for a fragment, derivative or analog of the polypeptide of Figures 1A-B or the polypeptide encoded by the cDNA of the deposited clone. Such nucleotide variants include deletion variants, substitution variants and addition or insertion variants.

At page 6, please delete the first full paragraph, which begins "As hereinabove indicated, the polynucleotide ...", and replace therewith the following paragraph:

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As hereinabove indicated, the polynucleotide may have a coding sequence which is a naturally occurring allelic variant of the coding sequence shown in Figures 1A-B (SEQ ID NO:1) or of the coding sequence of the deposited clone. As known in the art, an allelic variant is an alternate form of a polynucleotide sequence which may have a substitution, deletion or addition of one or more nucleotides, which does not substantially alter the function of the encoded polypeptide.

At page 7, please delete the last paragraph, extending onto page 8, which begins "The present invention further relates ...", and replace therewith the following paragraph:

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The present invention further relates to polynucleotides which hybridize to the hereinabove-described sequences if there is at least 70%, preferably at least 90%, and more preferably at least 95% identity between the sequences. The present invention particularly relates to polynucleotides which hybridize under stringent conditions to the hereinabove-described polynucleotides. As herein used, the term "stringent conditions" means hybridization will occur only if there is at least 95% and preferably at least 97% identity between the sequences. The polynucleotides which hybridize to the hereinabove described polynucleotides in a preferred embodiment encode polypeptides which either retain substantially the same biological function or activity as the mature polypeptide encoded by the cDNAs of Figures 1A-B (SEQ ID NO:1) or the deposited cDNA(s).

At page 9, please delete the first full paragraph, which begins "The present invention further relates ...", and replace therewith the following paragraph:

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The present invention further relates to an HDGF-2 polypeptide which has the deduced amino acid sequence of Figures 1A-B (SEQ ID NO:2) or which has the amino acid

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sequence encoded by the deposited cDNA, as well as fragments, analogs and derivatives of such polypeptide.

At page 9, please delete the second full paragraph, which begins "The terms 'fragment,' 'derivative' and ...", and replace therewith the following paragraph:

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The terms "fragment," "derivative" and "analog" when referring to the polypeptide of Figures 1A-B (SEQ ID NO:2) or that encoded by the deposited cDNA, means a polypeptide which retains essentially the same biological function or activity as such polypeptide. Thus, an analog includes a proprotein which can be activated by cleavage of the proprotein portion to produce an active mature polypeptide.

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At page 9, please delete the fourth full paragraph, which begins "The fragment, derivative or analog of...", and replace therewith the following paragraph:

The fragment, derivative or analog of the polypeptide of Figures 1A-B (SEQ ID NO:2) or that encoded by the deposited cDNA may be (i) one in which one or more of the amino acid residues are substituted with a conserved or non-conserved amino acid residue (preferably a conserved amino acid residue) and such substituted amino acid residue may or may not be one encoded by the genetic code, or (ii) one in which one or more of the amino acid residues includes a substituent group, or (iii) one in which the mature polypeptide is fused with another compound, such as a compound to increase the half-life of the polypeptide (for example, polyethylene glycol), or (iv) one in which the additional amino acids are fused to the mature polypeptide and employed for purification of the mature polypeptide. Such fragments, derivatives and analogs are deemed to be within the scope of those skilled in the art from the teachings herein.

At page 32, please delete the second full paragraph, which begins "The DNA sequence encoding HDGF-2...", and replace therewith the following paragraph:

Q¹⁶
The DNA sequence encoding HDGF-2, ATCC No. 97163, is initially amplified using PCR oligonucleotide primers corresponding to the 5' sequences of the protein and the vector sequences 3' to the gene. Additional nucleotides corresponding to the gene are added to the 5' and 3' sequences respectively. The HDGF-2 5' oligonucleotide primer has the sequence 5' ACGTGGATCCGCGGCTGTGAGTCTGCGGCTCGGC 3' (SEQ ID NO:3)

Q¹⁶ contains a BamHI restriction enzyme site. The 3' sequence 5' CAACAAGCTTTCACCTAGGAAGAAGGAGGTCTTCA 3' (SEQ ID NO:4) contains complementary sequences to a HindIII site and is followed by TGFa-HII coding sequence.

At page 33, please delete the first full paragraph, which begins "The DNA sequence encoding ...", and replace therewith the following paragraph:

Q¹⁷ The DNA sequence encoding the full length HDGF-2 protein, ATCC No. 97163, is amplified using PCR oligonucleotide primers corresponding to the 5' and 3' sequences of the gene:

At page 34, please delete the second full paragraph, extending onto page 35, which begins "The vector pA2 (modification of pVL941...", and replace therewith the following paragraph:

Q¹⁸ The vector pA2 (modification of pVL941 vector, discussed below) is used for the expression of the HDGF-2 protein using the baculovirus expression system (for review see: Summers, M.D. and Smith, G.E. 1987, A manual of methods for baculovirus vectors and insect cell culture procedures, Texas Agricultural Experimental Station Bulletin NO:1555). This expression vector contains the strong polyhedrin promoter of the Autographa californica nuclear polyhedrosis virus (AcMNPV) followed by the recognition sites for the restriction endonucleases. The polyadenylation site of the simian virus (SV)40 is used for efficient polyadenylation. For an easy selection of recombinant viruses the beta-galactosidase gene from E.coli is inserted in the same orientation as the polyhedrin promoter followed by the polyadenylation signal of the polyhedrin gene. The polyhedrin sequences are flanked at both sides by viral sequences for the cell-mediated homologous recombination of cotransfected wild-type viral DNA. Many other baculovirus vectors could be used in place of pA2 such as pRG1, pAc373, pVL941 and pAcIM1 (Luckow, V.A. and Summers, M.D., Virology, 170:31-39).

At page 35, please delete the first full paragraph, which begins "The plasmid is digested with ...", and replace therewith the following paragraph:

Q¹⁹ The plasmid is digested with the restriction enzymes and then dephosphorylated using calf intestinal phosphatase by procedures known in the art. The DNA is then isolated

Q¹⁹ from a 1% agarose gel using the commercially available kit ("Geneclean" BIO 101 Inc., La Jolla, Ca.). This vector DNA is designated V2.

At page 37, please delete the first full paragraph, which begins "The plasmid construction strategy...", and replace therewith the following paragraph:

Q²⁰ The plasmid construction strategy is described as follows:

At page 37, please delete the second full paragraph, which begins "The DNA sequence encoding HDGF-2,...", and replace therewith the following paragraph:

Q²¹ The DNA sequence encoding HDGF-2, ATCC No. 97163, contained in the plasmid vector pBluescript was amplified by PCR with a pBluescript vector primer (T3) at the 5' end and a HDGF-2 specific primer at the 3' end of the HDGF-2 coding sequence containing an XhoI restriction site. After amplification via PCR, the resultant PCR product is digested with BamHI and XhoI and ligated into a modified pcDNA-1 vector containing the HA tag in frame following the XhoI restriction site. The resultant plasmid contains the 5' untranslated region of HDGF-2 followed by the entire coding sequence fused in frame to the HA tag at the C-terminus.

In the Sequence Listing:

Please delete the original Sequence Listing (numbered pages 41-42) and renumber the Claims and Abstract (currently pages 43-46) as pages 41-44, respectively. Also, please append pages 1-7 of the Substitute Sequence Listing submitted herewith to the end of the present application.

In the Drawings:

Please replace the informal drawings of Figures 1 and 2 (3 sheets) with the Formal drawings of Figures 1A-1B and 2 (3 sheets) submitted herewith.